

## PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

VOSSIUS & PARTNER  
Siebenstrasse 4  
81675 München  
ALLEMAGNE**EINGEGANGEN**  
Vossius & Partner

12. DEZ. 2000

Frist:

1999

PCT

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT  
(PCT Rule 71.1)Date of mailing  
(day/month/year) 09.12.2000Applicant or agent's file reference  
C 1615 PCT

## IMPORTANT NOTIFICATION

International application No.  
PCT/EP99/06502International filing date (day/month/year)  
03/09/1999Priority date (day/month/year)  
03/09/1998

Applicant:

CPG IMMUNOPHARMACEUTICALS GMBH et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

## 4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/30\*).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the PEA:



European Patent Office  
D-60298 München  
Tel: +49 89 2369-0 Tx: 523696 eptm:c  
Fax: +49 89 2369-4465

Authorized officer:

Vullo, C

Tel: +49 89 2369-903\*




Form PCT/PEA/415 (July 1992)

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>C 1615 PCT</b>		<b>FOR FURTHER ACTION</b>		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)
International application No. <b>PCT/EP99/06502</b>		International filing date (day/month/year) <b>03/09/1999</b>	Priority date (day/month/year) <b>03/09/1998</b>	
International Patent Classification (IPC) or national classification and I.P. <b>C12N15/11</b>				
Applicant <b>CPG IMMUNOPHARMACEUTICALS GMBH et al.</b>				
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 9 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>				
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li>I <input checked="" type="checkbox"/> Basis of the report</li> <li>II <input type="checkbox"/> Priority</li> <li>III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li> <li>IV <input checked="" type="checkbox"/> Lack of unity of invention</li> <li>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability, citations and explanations supporting such statement</li> <li>VI <input type="checkbox"/> Certain documents cited</li> <li>VII <input type="checkbox"/> Certain defects in the international application</li> <li>VIII <input checked="" type="checkbox"/> Certain observations on the international application</li> </ul>				
Date of submission of the demand <b>26/02/2000</b>		Date of completion of this report <b>08/12/2000</b>		
Name and mailing address of the international preliminary examining authority:  <b>European Patent Office</b> <b>D-80289 Munich</b> <b>Te.: +49 89 2339-0 Fax: 513655 admu d</b> <b>Fax: +49 89 2339-4465</b>		Authorized officer  <b>Mooren, P</b> Telephone No. +49 89 2339 6536		

Form PCT/PEA/403 (cover sheet) (January 1994)

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP99/06502

**1. Basis of the report**

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rule 70.16 and 70.17).)*

**Description, pages:**

1-37 as originally filed

**Claims, No.:**

1-33 as originally filed

**Drawings, sheets:**

1/17-17/17 as originally filed

**Sequence listing part of the description, pages:**

1-14, as originally filed

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP99/06502

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:  
**see separate sheet**

**III. Non-establishment of opinion with regard to novelty, inventive step and Industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.  
☒ claims Nos. 22-30, 32-43.

because:

- ☒ the said international application, or the said claims Nos. 22-30, 32-33 relate to the following subject matter which does not require an international preliminary examination (*specify*):  
**see separate sheet**
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.  
☐ the computer readable form has not been furnished or does not comply with the standard.

**IV. Lack of unity of invention**

1. In response to the invitation to restrict or pay additional fees the applicant has:

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP99/06502

- ☐ restricted the claims.
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.
2. ☒ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
- ☐ complied with.
- ☒ not complied with for the following reasons:  
see separate sheet
4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:
- ☒ all parts.
- ☐ the parts relating to claims Nos. .

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

### 1. Statement

Novelty (N)	Yes: Claims 17, 22-26, 30-33
	No: Claims 1-16, 18-21, 27-29
Inventive step (IS)	Yes: Claims
	No: Claims 17, 22-26, 30-33
Industrial applicability (IA)	Yes: Claims 1-21 and 31
	No: Claims

### 2. Citations and explanations see separate sheet

## VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
see separate sheet

**INTERNATIONAL PRELIMINARY**

International application No. PCT/EP99/06502

**EXAMINATION REPORT - SEPARATE SHEET**

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Reference is made to the following documents:

- D1: WO 98 32462 A (LIPFORD GRAYSON II; HEEG KLAUS (DE); WAGNER HERMANN (DE)) 30 July 1998 (1998-07-30)
- D2: WO 96 24330 A (ICN PHARMACEUTICALS) 15 August 1996 (1996-08-15)
- D3: WO 98 29430 A (ICN PHARMACEUTICALS; TAM ROBERT (US)) 9 July 1998 (1998-07-09)
- D4: SPARWASSER, T. ET AL.: 'Bacterial DNA and immunostimulatory CpG oligonucleotides trigger maturation and activation of murine dendritic cells.' EUR J IMMUNOL 1998 JULN;28(6):2045-54
- D5: BALLAS, Z. ET AL.: 'INDUCTION OF NK ACTIVITY IN MURINE AND HUMAN CELLS BY CPG MOTIFS IN OLIGODEOXYNUCLEOTIDES AND BACTERIAL DNA' JOURNAL OF IMMUNOLOGY, vol. 157, no. 5, September 1996 (1996-09), page 1840-1845
- D6: KIMURA Y ET AL.: 'BINDING OF OLIGOGUANYLATE TO SCAVENGER RECEPTORS IS REQUIRED FOR OLIGONUCLEOTIDES TO AUGMENT NK CELL ACTIVITY AND INDUCE IFN' JOURNAL OF BIOCHEMISTRY, vol. 116, no. 5, November 1994 (1994-11), pages 991-994
- D7: KRIEG, A.: 'Leukocyte stimulation by oligodeoxynucleotides' STEIN, C.A. & KRIEG, A.M. 'APPLIED ANTISENSE OLIGONUCLEOTIDE TECHNOLOGY'. WILEY-LISS, NEW YORK, US;1998; CHAPTER 24, pages 431-448
- D8: WLOCH ET AL.: 'THE INFLUENCE OF DNA SEQUENCE ON THE IMMUNOSTIMULATORY PROPERTIES OF PLASMID DNA VECTORS' Hum Gene Ther 9 (Jul 1, 1998) 1439-47; abstract only \*

- \* The document D8 was not cited in the international search report. A copy of the document has been sent to the Applicant.

**Re Item I****Basis of the opinion**

1. The sequence listing, separately numbered in the published application WO 00/14217 as pages 1-14, has been taken into account for this opinion.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP99/06502

**Re Item III****Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

2. For the assessment of the present claims 22-30 and 32-33 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Claims 22-30 and 32-33 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(i) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

**Re Item IV****Lack of unity of invention**

3. **Introduction:** the present application concerns G-motif oligonucleotides having the sequence  $N_1-N_2-G-N_3-G$  in which one of the three nucleotides N can be any nucleotide, and the other two N nucleotides are G, and their use in the modulation of the immune system. The definition includes e.g. the sequences GGGGG and GGGGCG also referred to in D1 (preferred immunomodulatory sequences mentioned on page 25 Table 4, EGR and SP1, respectively), as well as sequences referred to in e.g. D2 (claims 14-15), D3 (top of page 10), D6 (oligoG) and D7 (see Table 42.2, e.g. Antisense TGF- $\beta$ ).
4. It is therefore considered that between the differently claimed sequences in claims 3 and 4 a single general inventive concept (referred to in Rule 13 PCT and the PCT Preliminary Examination Guidelines Ch.III, 7) is not recognisable in the absence of a common, special technical feature. Non-unity may also be present between the different set of claims for medical treatment.

**INTERNATIONAL PRELIMINARY**

International application No. PCT/EP99/06502

**EXAMINATION REPORT - SEPARATE SHEET****Re Item V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

5. As mentioned above the (single stranded) sequence GGGGG is referred to in D1 within a sequence of 20 nucleotides. Therefore, the present application does not satisfy the criterion set forth in Article 31(2) PCT because the subject-matter of **claims 1-3, 5-7, 10-14, 18-21 and 27** is not new in respect of prior art as defined in the regulations (Rule 64(1)(3) PCT); with respect to claims 14 and 27, your attention is drawn to claims 16 and 22 of D1, and with respect to present claims 20-21 to description page 15 lines 1-7 and claim 21 of D1. D1 contains also a (single stranded) GGGGGCG sequence representing the 3'-terminus of the EGR-derived oligonucleotide, and is therefore prejudicial to the novelty of **claim 8**. **Claims 15-16** lack also novelty over D1.
6. **Claims 4 and 9** refer to twenty sequences in majority of 21 base pairs and SEQ ID NOs: 1 to 19; these sequences appear to be new, except for SEQ ID NO:17 (see D2, claim 9, SEQ ID NO:3) and SEQ ID NO:18-19 (see D1, Table 4, elements SP1 and EGR). These claims therefore lack novelty. With respect to the apparently new sequences it is noted that they do not involve an inventive step over D1. Said sequences have a close structural identity with the sequences specified in D1 (as well as D2 and D3) and a particular advantage of the presently claimed sequences is not exemplified; in particular it is noted that e.g. SEQ ID NO:1 is not tested for the inhibitory concentration  $IC_{50}$  (no mentioning in the Tables 1-6).
7. **Claim 17** refers to a method for production of an oligonucleotide in a host cell. This is standard practice at the priority date and therefore this claim does not involve an inventive step.
8. With respect to **claims 22-23** attention is drawn to the disclosure of D4 concerning the immunostimulatory CpG ODN, triggering maturation and activation of murine dendritic cells. In view of D1, considered to be the closest prior art document, in combination with the teaching of D4 it is considered that the subject-matter of **claims 22-23** is obvious.



**INTERNATIONAL PRELIMINARY**

International application No. PCT/EP99/06502

**EXAMINATION REPORT - SEPARATE SHEET**

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9. **Claim 24:** no prior art referred or suggested the claimed subject-matter. However, an involvement of an inventive step is denied as it is not clear if the technical problem is solved over the whole range of sequences of the ODNs of the invention; example 3 and Figure 3 refer to the term "G-motif ODN", which is defined as the ODN of the present invention and/or ODN to be employed in accordance with the composition of the present invention. It is therefore not clear which ODN has or have been tested.
10. D3 discloses inducing NK lytic activity by CpG motif containing ODN. Taken the disclosure of D1 in combination with the teaching of D5 it is therefore considered that the subject-matter of **claims 25-26** lack an inventive step.
11. **Claims 28-30** refer to the enhancing of the uptake of an agent by a cell: D1 has referred to the increased expression of the IL-2 receptor. This leads also to an increased uptake of IL-2. Claims 28-29 lack therefore novelty over D1. The enhancement of uptake of a gene therapy vector by a (vertebrate) cell: in view of the fact that the documents like D1 and D2 refer to the uptake of the ODN of the present application it is considered that the subject-matter of claim 30 is obvious to the skilled person, in particular in combination with the teaching of D8.
12. **Claims 31-33** refer to the induction of proliferation of bone marrow cells: D4 has referred to the triggering of immature (bone marrow derived) dendritic cells to mature dendritic cells, the trigger being bacterial DNA and immunostimulatory CpG. In view of D1 and D4 it is therefore considered that claims 31-33 lacks an inventive step.

**Re Item VIII****Certain observations on the international application**

13. In conjunction with the above observation with respect to the lack of unity of invention, it is noted that Article 6 of the PCT requires that all independent claims contain the essential technical feature(s) of the invention (see also Rule 6.3(b) PCT)

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/EP99/06502

At present the special technical feature of the invention, present in all independent claims on file, is not recognisable.

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## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
 United States Patent and Trademark  
 Office  
 Box PCT  
 Washington, D.C. 20231  
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

<b>Date of mailing</b> (day/month/year) 13 April 2000 (13.04.00)	
<b>International application No.</b> PCT/EP99/06502	<b>Applicant's or agent's file reference</b> C 1615 PCT
<b>International filing date</b> (day/month/year) 03 September 1999 (03.09.99)	<b>Priority date</b> (day/month/year) 03 September 1998 (03.09.98)
<b>Applicant</b> WAGNER, Hermann et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
 28 February 2000 (28.02.00)

☐ in a notice effecting later election filed with the International Bureau on:  
 \_\_\_\_\_

2. The election ☒ was  
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<b>The International Bureau of WIPO</b> 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Nestor Santesso Telephone No.: (41-22) 338.83.38
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PATENT COOPERATION TREATY

1 09/786 436

PCT

From the INTERNATIONAL BUREAU

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

To:

VOSSIUS & PARTNER  
P.O. Box 86 07 67  
D-81634 Munich  
ALLEMAGNE

Date of mailing (day/month/year) 26 February 2001 (26.02.01)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference C 1615 PCT	
International application No. PCT/EP99/06502	International filing date (day/month/year) 03 September 1999 (03.09.99)

1. The following indications appeared on record concerning:		
<input checked="" type="checkbox"/> the applicant	<input type="checkbox"/> the inventor	<input type="checkbox"/> the agent <input type="checkbox"/> the common representative
Name and Address CPG IMMUNOPHARMACEUTICALS GMBH c/o Qiagen GmbH Max-Volmer-Strasse 4 D-40724 Hilden Germany	State of Nationality DE	State of Residence DE
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:		
<input checked="" type="checkbox"/> the person	<input type="checkbox"/> the name	<input type="checkbox"/> the address <input type="checkbox"/> the nationality <input type="checkbox"/> the residence
Name and Address COLEY PHARMACEUTICAL GMBH Elisabeth-Selbert-Strasse 9 D-40764 Langenfeld Germany	State of Nationality DE	State of Residence DE
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
3. Further observations, if necessary:		
4. A copy of this notification has been sent to:		
<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned	
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned	
<input type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:	

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer  Elisabeth KÖNIG
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>C 1615 PCT</b>		<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, Item 5 below.	
International application No. <b>PCT/EP 99/ 06502</b>	International filing date (day/month/year) <b>03/09/1999</b>	(Earliest) Priority Date (day/month/year) <b>03/09/1998</b>	
Applicant <b>CPG IMMUNOPHARMACEUTICALS GMBH et al.</b>			

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☒ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. ☒ Certain claims were found unsearchable (See Box I).

3. ☐ Unity of invention is lacking (see Box II).

## 4. With regard to the title,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

## 5. With regard to the abstract,

☐ the text is approved as submitted by the applicant.

☒ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

## 6. The figure of the drawings to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP 99/06502

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claims 22-26, 28-30, 32-33 (as far as in vivo methods are concerned) are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/EP 99/06502

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/11 A61K39/39 A61K31/70 C07H21/04 //A61K45/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 32462 A (LIPFORD GRAYSON B ;HEEG KLAUS (DE); WAGNER HERMANN (DE)) 30 July 1998 (1998-07-30) page 9, line 7 -page 12, line 7 page 14, paragraph 2 -page 15, paragraph 2 examples 1,5,7	1-23
Y	claims	25, 26, 28-30
Y	KIMURA Y ET AL: "BINDING OF OLIGOGUANYLATE TO SCAVENGER RECEPTORS IS REQUIRED FOR OLIGONUCLEOTIDES TO AUGMENT NK CELL ACTIVITY AND INDUCE IFN" JOURNAL OF BIOCHEMISTRY, vol. 116, no. 5, November 1994 (1994-11), pages 991-994, XP000616565 ISSN: 0021-924X the whole document	25, 26, 28-30

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Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## \* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&amp;" document member of the same patent family

Date of the actual completion of the international search

23 February 2000

Date of mailing of the international search report

13/03/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 99/06502

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>BALLAS, Z. ET AL.: "INDUCTION OF NK ACTIVITY IN MURINE AND HUMAN CELLS BY CPG MOTIFS IN OLIGODEOXYNUCLEOTIDES AND BACTERIAL DNA" JOURNAL OF IMMUNOLOGY, vol. 157, no. 5, September 1996 (1996-09), page 1840-1845 XP002053416 ISSN: 0022-1767 abstract page 1841, right-hand column, last paragraph -page 1842 page 1844, left-hand column, last paragraph -page 1845</p> <p>---</p>	1-3, 5-12, 18, 20, 25, 26
X	<p>WO 96 24380 A (ICN PHARMACEUTICALS) 15 August 1996 (1996-08-15) page 5, paragraph III. page 13, line 32 -page 14, line 20 page 19, last paragraph -page 24, paragraph 6 page 26 -page 27 page 31, paragraph 2 -page 32, line 7 page 45 -page 47, line 5</p> <p>---</p>	1-13, 15-22
X	<p>WO 98 29430 A (ICN PHARMACEUTICALS ;TAM ROBERT (US)) 9 July 1998 (1998-07-09)</p> <p>page 8 -page 10 page 26; table 1 claims</p> <p>---</p>	1-3, 5-13, 18-21
A	<p>KRIEG, A.: "Leukocyte stimulation by oligodeoxynucleotides" STEIN, C.A. &amp; KRIEG, A.M. 'APPLIED ANTISENSE OLIGONUCLEOTIDE TECHNOLOGY'. WILEY-LISS, NEW YORK, US;1998; CHAPTER 24, pages 431-448, XP002131392 page 444, line 19 -page 445</p> <p>---</p>	1-33
A	<p>SPARWASSER, T. ET AL.: "Bacterial DNA and immunostimulatory CpG oligonucleotides trigger maturation and activation of murine dendritic cells." EUR J IMMUNOL 1998 JUN;28(6):2045-54, XP002131393 the whole document</p> <p>---</p>	22, 23
A	<p>KRIEG A M ET AL: "THE ROLE OF CpG DINUCLEOTIDES IN DNA VACCINES" TRENDS IN MICROBIOLOGY, vol. 6, no. 1, January 1998 (1998-01), pages 23-26, XP000857633 ISSN: 0966-842X</p> <p>---</p>	
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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	<p>LANG R. ET AL.: "Guanosine-rich oligodeoxynucleotides induce proliferation of macrophage progenitors in cultures of murine bone marrow cells."            EUR J IMMUNOL 1999 NOV;29(11):3496-506, XP000876859</p> <p>-----</p>	
T	<p>PISETSKY DS. ET AL.: "The influence of base sequence on the immunostimulatory properties of DNA."            IMMUNOL RES 1999;19(1):35-46, XP000884065</p> <p>-----</p>	

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Information on patent family members

International Application No.

PCT/EP 99/06502

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## Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

The present invention relates to a composition an oligonucleotide comprising (a) the sequence N1 - N2 - G - G3 - G, wherein N1 represents any nucleotide if N2 and N3 are G; N2 represents any nucleotide if N1 and N3 are G; and N3 represents any nucleotide if N1 and N2 are G, or (b) the sequence of (a), wherein at least one nucleotide is replaced by a corresponding nucleotide analog or derivative.

The present invention further relates to the use of the composition, and/or the oligonucleotide of the present invention for the production of a pharmaceutical composition for preventing or treating septic shock, inflammation, autoimmune diseases, Th1-mediated diseases, bacterial infections, parasitic infections, viral infections, spontaneous abortions, and/or tumors.